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VASCULAR DISEASE

SNPS IN NOS3 ARE ASSOCIATED WITH A CARDIOVASCULAR DISEASE SCORE IN ASYMPTOMATIC INDIVIDUALS

ACC Poster Contributions
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Background: A cardiovascular disease (CVD) score based on the sum of the scores of 10 functional and structural markers for early CVD is more predictive for CVD morbid events than the traditional Framingham risk score in subjects free of overt CVD. Endothelial dysfunction plays a key role in the pathogenesis of cardiovascular disease. We examined the association of SNPs in NOS3 with this CVD score.

Methods: A total of 536 subjects (356 males, 180 females) free of overt CVD underwent 10 noninvasive tests for function and structure of the blood vessels and the heart: 1) large and 2) small artery elasticity derived from diastolic pulse contour analysis of the radial artery waveform using tonometry; 3) resting arterial blood pressure 4) blood pressure response at the end of a 3 min exercise treadmill test; 5) retinal photography 6) carotid intima-medial thickness with ultrasound; 7) micro-albuminuria 8) ECG; 9) Brain-Natriuretic Peptide; and 10) left ventricular wall thickness and diameters by cardiac ultrasonography. Each test was score as 0 if normal, 1 if borderline and 2 if abnormal. The CVD score was the sum of the 10 tests (range can be between 0 and 20). A blood sample was taken and 9 tagging SNPs in NOS3 were genotyped using Sequenom with a call rate > 99.5%. Linear regression analysis was performed using PLINK software, with age, sex and BMI as covariates. All SNPs were in Hardy-Weinberg equilibrium. Haplotypes of NOS3 were constructed using the Gabriel method.

Results: A significant association was identified in the haplotype block containing 2 SNPs rs1799983 (Glu298Asp) and rs3918227, decreased systolic blood pressure ($p < 0.05$) and a decrease in the overall CVD score ($p < 0.047$). A second haplotype block including SNPs rs1808593 and rs7830 was also associated with a decrease in the overall CVD score ($p < 0.045$).

Conclusions: These results suggest that DNA variants in NOS3 are associated with decreased systolic blood pressure and improvement in a CVD score in asymptomatic subjects. Future studies are needed to replicate these findings and further define the genetic structure of NOS3 and how this influences its regulation.